158. The method according to claim 155, wherein said probes contain nucleic acid segments which are substantially complementary to nucleic acid segments that extend fully across breakpoint regions known to be associated with genetic translocations.

~~159~~ 24. The method according to claim ~~150~~ 19, wherein said probes contain nucleic acid segments which are substantially complementary to nucleic acid segments that flank breakpoint regions known to be associated with genetic translocations.

~~160~~ 25. The method according to claim ~~150~~ 19, wherein said probes contain nucleic acid segments which are substantially complementary to nucleic acid segments that extend partially across breakpoint regions known to be associated with genetic translocations.

~~161~~ 26. The method according to claim ~~150~~ 19, wherein said probes contain nucleic acid segments which are substantially complementary to nucleic acid segments that extend fully across breakpoint regions known to be associated with genetic translocations.

REMARKS

Entry of the foregoing, reexamination and reconsideration of the above-identified application are respectfully requested.

New claims 154-161 have been added, directed to preferred embodiments of the instant invention. Support for claim 154 may be found at the very least at page 20, lines 13-17. Support for new claims 155-161 may be found at the very least in claim 150

and at page 35, lines 6-8 and lines 20-24; page 40, lines 12-13; page 74, line 18 - page 75, line 18; and in the Examples.

Claims 131-153 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly containing new matter. This rejection is respectfully traversed.

According to the Examiner, the citations of support in the application for the recitation of "40 kb" allegedly refer to "probe length and not its complexity." This assertion is believed to be in error. By reference to the specification, it can be seen that the recitation of 40 kb refers to probe complexity as claimed.

For example, at the very least at page 37, line 13 to page 38, line 13, the specification is discussing complexity of the probe:

> The term "*complexity*" is defined herein according to the standard for nucleic acid complexity as established by Britten et al., Methods of Enzymol., 29:363 (1974). See also Cantor and Schimmel, Biophysical Chemistry: Part III: The Behavior of Biological Macromolecules, at 1228-1230 (Freeman and Co. 1980) for further explanation and exemplification of nucleic acid complexity.
>
> The *complexity* preferred for a probe composition of this invention is dependent upon the application for which it is designed. In general, the larger the target area, the more complex is the probe. It is anticipated that the *complexity* of a probe needed to produce a desired pattern of landmarks on a chromosome will decrease as hybridization sensitivity increases, as progress is made in hybridization technology. As the sensitivity increases, the reliability of the signal from smaller target sites will increase. Therefore, whereas from about a 40 kb to about a 100 kb target sequence may be presently necessary to provide a reliable, easily detectable signal, smaller target sequences should provide reliable signals in the future. Therefore, as hybridization sensitivity increases, a probe of a certain *complexity*, for example, 100 kb, should enable the user to detect considerably more loci in a genome than are presently reliably detected; thus, more information will be obtained with a probe of the same complexity. The term "*complexity*" therefore refers to the *complexity* of the

total probe no matter how many visually distinct loci are to be detected, that is, regardless of the distribution of the target sites over the genome.

As indicated above, with current hybridization techniques it is possible to obtain a reliable, easily detectable signal with a probe of about 40 kb to about 100 kb (eg. the probe insert capacity of one or a few cosmids) targeted to a compact point in the genome. Thus, for example, a *complexity* in the range of approximately 100 kb now permits hybridization to both sides of a tumor-specific translocation. (Italic emphasis supplied).

It is clear from the context of the application that complexity of the probe, and not length as alleged by the Examiner, is being discussed for the recitation of "40 kb." More specifically, for example, at page 37, lines 13-17, the term "complexity" is defined. At page 37, lines 18-23, immediately prior to the recitation of "40 kb", the specification discusses the "complexity of a probe needed to produce a desired pattern of landmarks on a chromosome." At page 38, lines 5-7, immediately following the recitation of "40 kb", the application again discusses "complexity" of the probe. Similarly, immediately after the recitation of "a probe of about 40 kb", the specification states "a complexity in the range of approximately 100 kb" (*see,* page 38, lines 8-13).

By review of the description in the specification of "40 kb," it is clear that complexity is being referenced. No new matter is thus being added by these claims reciting a complexity of "40 kb."

Regarding claim 145, it was believed to be clear that the "50" was 50 kb since it indicated a range for complexity of the probe. However, to expedite prosecution, the claim has been amended to recite "50 kb."

I

Claim 139 also allegedly contains new matter in view of the recitation of "no more than 1 micron." While the claims as written is believed to be fully supported by the specification, to expedite prosecution on the merits, claim 139 has been amended to recite "less" than 1 micron.

In view of the above, withdrawal of the rejection of the claims under 35 U.S.C. §112, first paragraph, is respectfully requested and believed to be in order.

Claims 136, 144, 145 and 150-153 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. This rejection is now moot in view of the instant amendment. The Examiner has objected to the recitation of a range which does not recite the units after the first number. It is believed to be clear that both the first and second numbers in the ranges refer to "kb." To expedite prosecution on the merits, the claims have been amended to recite "kb" after both the first and second numbers.

Claims 150-153 were objected to as being unclear in view of the recitation of "a distinct label" and multiple "nucleic acid probes." This aspect of the rejection is now moot in view of the amendment to claim 150.

Applicants appreciate the Examiner's return of the signed PTO Form 1449. It was believed that a copy of each cited reference was included. In the event that copies of certain references were separated from the file, copies of those references are enclosed herewith. An additional PTO 1449 Form is also enclosed, listing only those references enclosed herewith. Return of the additional PTO 1449 Form, initialed by the Examiner, is respectfully requested.

Further and favorable action in the form of a Notice of Allowance is respectfully requested.

In the event that there are any questions relating to this response, or to the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____
Donna M. Meuth
Registration No. 36,607

Post Office Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: June 4, 1998